

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2005/000140

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. ⁷: C12N 15/12, C07K 14/435

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MEDLINE, CAPLUS, BIOSIS, WPIDS, BIOTECHABS (BH3 only, Bcl-2, antagonist, inhibit)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X | Adachi, M and Imai, K.; Cell Death and Differentiation, (2002 Nov) 9 (11) 1240-7 "The proapoptotic BH3 - only protein BAD transduces cell death signals independently of its interaction with Bcl-2. (Whole document) | 1-7, 9-17 and 18 |
| X | Yamaguchi, H., et al; Journal of Biological Chemistry, (2002 Nov 1) 277 (44) 41604-12. "Bcl-XL protects BimEL-induced Bax conformational change and cytochrome C release independent of interacting with Bax or BimEL. (Whole document) | 1-7, 9-17 and 18 |
| X | Wang, K., et al; Genes and Development, (1996 Nov 15) 10 (22) 2859-69. "BID: a novel BH3 domain-only death agonist." (Whole document) | 1-7, 9-17 and 18 |

 Further documents are listed in the continuation of Box C See patent family annex

| | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| * Special categories of cited documents: | | |
| "A" document defining the general state of the art which is not considered to be of particular relevance | "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| "E" earlier application or patent but published on or after the international filing date | "X" | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | "Y" | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "O" document referring to an oral disclosure, use, exhibition or other means | "&" | document member of the same patent family |
| "P" document published prior to the international filing date but later than the priority date claimed | | |

Date of the actual completion of the international search
25 February 2005

Date of mailing of the international search report

02 MAR 2005

Name and mailing address of the ISA/AU

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| C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|-------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | Baell, J. B., and Huang D. C. S.; Biochemical Pharmacology, (2002 Sep) 64 (5-6) 851-63. "Prospects for targeting the Bcl-2 family of proteins to develop novel cytotoxic drugs." (Whole document) | 1-7, and 9-18 |
| A | Bettaieb, A., et al; Current Medicinal Chemistry Anti-cancer Agents, (2003 Jul) 3 (4) 307-18 "Bcl - 2 proteins: targets and tools for chemosensitisation of tumor cells." (Abstract, pages 310, 311, 313 and 314) | 1-18 |
| A | WO 2002/097094 A1 (THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH) 05.12.2002 (Whole document) | 1-18 |
| A | WO 2003/028443 A1 (THE WALTER AND ELIZA HALL INSTITUTE OF MEDICAL RESEARCH) 10.04.2003 (Whole document) | 1-18 |

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: **12-16 in part.** because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
Claims 12-16 are not restricted to the technical features of the invention.
(continued)

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

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Supplemental Box II

(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No 2:

The claims 12 and 13 include all Bcl-2 proteins and also define computers for assessing features associated with all Bcl-2 proteins which do not form the basis of the invention. The invention relates to antagonists for pro-survival Bcl-2 proteins that are based on the BH3-only protein structure. Bcl-2 proteins include all Bcl-2 family members which include anti-apoptotic members, pro-apoptotic members and members of the BH3-only proteins. The invention, however, is restricted to BH3-only proteins. The proteins are used as a scaffold for changing residues in the amphipathic α -helix of the BH3-only proteins such that a promiscuous binding phenotype of the BH3-only protein is converted to a restrictive binding phenotype. Therefore only parts of the claims relating to the BH3-only proteins were searched.

Claims 14-16 include any antagonist for Bcl-2 proteins irrespective of whether they are derived from the BH3-only proteins, the invention, however, is restricted to BH3-only mimetics/variants as antagonists for pro-survival Bcl-2 proteins

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This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

| Patent Document Cited in Search Report | | Patent Family Member | | |
|-------------------------------------------|----------|----------------------|---------|------------|
| WO | 02097094 | CA | 2449000 | EP 1402032 |
| WO | 03028443 | | | |

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

END OF ANNEX